

CLAIMS:

1. A system for assaying one or more targets in a sample, comprising:

- 5 (a) an assay device having one or more assay sets at least one for each target to be assayed; each of the assay sets comprising at least two electrodes and a recognition moiety immobilized either to one or more of the at least two electrodes and/or onto a substrate between the at least two electrodes; the recognition moiety being capable of specific binding to one of the targets;
- 10 (b) an electric or electronic module for determining electric conductance between the at least two electrodes of each assay set; and
- (c) reagents for growing a conducting substance from nucleation centers-forming entities deposited onto or bound to a complex formed between said recognition moiety and said target, which substance forms a conductive
- 15 bridge between at least two of the electrodes of a set.

2. A system according to Claim 1, wherein said reagents comprise:

- (c1) a solution comprising nucleation-centers forming entities for binding to said target if present in the sample; and
- (c2) a combination of metal ions and a reducing agent to allow growth
- 20 of said metal substance on said entities.

3. A system according to Claim 1, wherein said reagents comprise:

- (c1) one or more reagents to allow deposition and/or formation of said nucleation center-forming entities on a complex formed between said recognition moiety and said target; and
- 25 (c2) a combination of metal ions and a reducing agent to allow growth of said metal substance from said entities.

4. A system according to Claim 2 ~~or 3~~, wherein said nucleation-center forming entities are colloid particles.

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5. A system according to Claim 2 ~~or 3~~, wherein said nucleation-center forming entities are metal complexes and/or clusters.

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DA 6. A system according to Claim 4, wherein said colloid particles are colloid gold particles.

5 7. A system according to Claim 5, wherein said metal complexes and/or clusters are gold complexes and/or clusters.

8. A system according to Claim 4, wherein said colloid particles are colloid platinum particles.

9. A system according to Claim 5, wherein said metal complexes and/or clusters are platinum complexes and/or clusters.

10 10. A system for assaying one or more targets in a sample, comprising:

(a) an assay device having one or more assay sets at least one for each target to be assayed; each of the assay sets comprising at least two electrodes and
15 a recognition moiety immobilized either to one or more of the at least two electrodes and/or on a substrate between the at least two electrodes; the recognition moiety being capable of specific binding to one of the targets;

(b) an electric or electronic module for determining electric conductance between the at least two electrodes of each assay set; and

20 (c) reagents comprising monomers of a conducting polymer which can bind to a complex formed between said recognition moiety and said target, such that upon polymerization of the monomers a conducting bridge between the at least two electrodes of a set is formed.

11. A system according to Claim 6, wherein said monomers are
25 monomers of polyaniline.

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DA 12. A system according to any one of the preceding claims, wherein said one or more targets are one or more nucleic acid sequences.

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13. A system according to Claim 12, wherein said recognition moiety is an oligonucleotide having a sequence complementary to at least a portion of sequence of one of said one or more targets.
14. A system according to ~~any one~~ of the preceding claims, wherein a
5 recognition moiety is immobilized on at least one electrode of each assay set.
15. A system according to Claim 14, wherein at least two electrodes of the assay set have each a recognition moieties immobilized thereon, these recognition moieties, being the same or different, bind specifically to the same target.
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- 10 16. A system according to Claim 14 ~~or 15~~, wherein the recognition moiety is immobilized onto the electrode by means of a linker conjugated or complexed with the recognition moiety and attached by a covalent or non covalent bond, to the electrode.
17. A system according to ~~any one~~ of the preceding claims, wherein
15 the recognition moiety is immobilized on a carrier substrate which is other than the electrode.
18. A system according to ~~any one~~ of the preceding claims, comprising a plurality of assay sets of electrodes.
19. A system according to Claim 18, wherein all assay sets of
20 electrodes are for assaying the same target.
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20. A system according to Claim 18, wherein different assay sets of electrodes or different groups of assay sets are for assaying different targets.
21. A system according to Claim 20, for simultaneous determination at different targets in a sample.
- 25 22. A system according to ~~any one of Claims 1-11~~, when the target is a protein or polypeptide and the recognition moiety is a protein-binding molecule which specifically binds to the target protein.

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23. A system according to Claim 22, wherein said recognition moiety is an antibody or antibody fraction comprising at least the antigen-binding domain of the antibody.

24. A method for assaying one or more targets in a sample comprising:

5 (a) providing an assay device having one or more assay sets at least one for each target to be assayed; each of the assay sets comprising at least two electrodes and a recognition moiety immobilized either to one or more of the at least two electrodes and/or on a substrate between the at least two electrodes; the
10 recognition moiety being capable of specific binding to one of the targets;

(b) contacting said assay device with said sample under conditions permitting binding of targets to specific recognition moieties;

(c) contacting said device with a first reagent solutions to form nucleation-center forming entities on complexes formed between a target and a
15 recognition moiety;

(d) connecting said device with a second reagent solution to grow a conducting metal substance from said nucleation center for a time sufficient to yield a conductive bridge between said at least two electrodes;

(e) connecting said at least two electrodes to an electric or electronic
20 module to measure conductance between said at least two electrodes; and

(f) determining conductance between said at least two electrodes, conductance above a threshold conductance indicating the presence of a respective target in the sample.

25 25. A method for assaying one or more targets in a sample, comprising:

(a) reacting the sample targets with a first reagent solution to bind nucleation-center forming entities to said targets;

(b) providing an assay device having one or more assay sets at least one for each target to be assayed; each of the assay sets comprising at least

two electrodes and a recognition moiety immobilized either to one or more of the at least two electrodes and/or on a substrate between the at least two electrodes; the recognition moiety being capable of specific binding to one of the targets;

5 (c) contacting said assay device with said sample under conditions permitting binding of targets to specific recognition moieties;

(d) contacting said device with a second reagent solution to grow a conducting metal substance from said nucleation center for a time sufficient to yield a conductive bridge between said at least two electrodes;

10 (e) connecting said at least two electrodes to an electric or electronic module to measure conductance between said at least two electrodes; and

(f) determining conductance between said at least two electrodes, conductance above a threshold conductance indicating the presence of a respective target in the sample.

15 26. A method for assaying one or more targets in a sample, comprising:

(a) providing an assay device having one or more assay sets at least one for each target to be assayed; each of the assay sets comprising at least two electrodes and a recognition moiety immobilized either to one or more of the at
20 least two electrodes and/or on a substrate between the at least two electrodes; the recognition moiety being capable of specific binding to one of the targets;

(b) contacting said assay device with said sample under conditions permitting binding of targets to specific recognition moieties;

(c) contacting said device with a first reagent solution comprising
25 monomers of a conductive polymer such that said monomers can bind to complexes formed between the targets and recognition moieties;

(d) treating said device such that said monomers will polymerize to form a conducting polymer, and thereby forming a conducting bridge between at least two electrodes of at least one assay set; and

(e) determining a conductance between said at least two electrodes, conductance above a threshold conductance indicating the presence of a respective target in the sample.

27. A method according to Claim 26, comprising the following step

5 (a₀) before step (a):

(a₀) reacting the sample with a second reagent solution containing entities which can form nucleation centers for growing therefrom a conductive polymer from said monomers, such that said entities bind to said targets if present in the sample.

10 28. A method according to Claim 26, comprising the following step

(a₁) after step (a):

(a₁) contacting said assay device with a second reagent solution containing entities which can form nucleation centers for growing therefrom a conductive polymer from said monomers, such that said entities bind to said targets if bound to said recognition moieties.

15 29. A method according to ~~any one of Claims 24 to 28~~, wherein said targets are nucleic acid sequences and the recognition moieties are oligonucleotides, each of which has a sequence which is complementary to one of the sequences of said targets.

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20 30. A method according to ~~any one of Claims 24 to 29~~, wherein the level of determining conductance serves as a measure of concentration of the target in the sample.

31. A kit for use in assaying one or more targets in a sample, comprising:

25 (a) an assay device having one or more assay sets at least one for each target to be assayed; each of the assay sets comprising at least two electrodes and a recognition moiety immobilized either to one or more of the at least two electrodes and/or onto a substrate between the at least two electrodes; the recognition moiety being capable of specific binding to one of the targets; and

(b) reagents for growing a conducting substance from nucleation centers-forming entities deposited onto or bound to a complex formed between said recognition moiety and said target, which substance forms a conductive bridge between at least two of the electrodes of a set.

5 32. A kit according to Claim 31, where said reagents comprise:

(b₁) a solution comprising nucleation-centers forming entities for binding to said target if present in the sample; and

(b₂) a combination of metal ions and a reducing agent to allow growth of said metal substance on said entities.

10 33. A kit according to Claim 31, where said reagents comprise:

(b₁) one or more reagents to allow deposition and/or formation of said nucleation-center forming entities on a complex formed between said recognition moiety and said target; and

(b₂) a combination of metal ions and a reducing agent to allow growth of said metal substance from said entities.

15 34. A kit for use in assaying one or more targets in the sample comprising:

(a) an assay device having one or more assay sets at least one for each target to be assayed; each of the assay sets comprising at least two electrodes and
20 a recognition moiety immobilized either to one or more of the at least two electrodes and/or onto a substrate between the at least two electrodes; the recognition moiety being capable of specific binding to one of the targets; and

(b) reagents comprising monomers of a conducting polymer which can bind to the target or to a complex formed between said recognition moiety
25 and said target, such that upon polymerization of the monomers a conducting bridge between the at least two electrodes of a set is formed.

35. An electronic device for determining one or more targets in a sample, comprising:

an integrated circuit comprising the first group of N_1 conductors and a second group of N_2 conductors, defining between them $N_1 \times N_2$ junctions, each such junction being formed with an electronic module comprising two electrodes, each one linked to or defined as an integral portion of one of the conductors, and comprises a diode or non-linear component permitting current flow through the electronic module only in the direction from the first group of conductors to the second group of conductors, whereby a current flowing between one conductor of the first group to one conductor of the second group of conductors defines a single junction point between them; each pair of electrodes forming part of an assay set, each assay set having a recognition moiety bound either to at least one of the electrodes or to a non-conducting substance disposed between the electrodes.

36. A device according to Claim 35, wherein distance of center of one assay set to a center of an adjacent assay set is 100 μM or less.

15 37. An electric device for determining one or more targets in a sample, comprising

a microelectronic device having a plurality of layers, with a first group of conductors being defined as stripes in one or more first layers and a second group of conductors being defined as stripes in one or more second layers of the device with each of said second layers being separated from a first layer by a non-conducting substance, electrodes of the device being formed as open ends of the conductors by openings or cut-outs in a vertical direction through the layers;

each pair of electrodes forming part of an assay set, each assay set having a recognition moiety bound either to at least one of the electrodes or to a non-conducting substance present between the electrodes.

25 38. A system according to any one of Claims 18 to 23, wherein the device is that defined according to any one of Claims 35 to 37.

39. A method according to any one of Claims 24 to 30, wherein said device is a device according to any one of Claims 35 to 37.

40. A method according to Claim 39, wherein said device has a plurality of assay sets for each target to be assayed, the method comprising
5 determining the proportion of assay sets displaying a conductance above thresholds, out of all assay sets for one target and based on such determination determining concentration of the target in the sample.

41. A method for detecting one or more targets in a sample by multiplexing comprising:

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10 (i) contacting the electronic device of Claim 35 with the sample under conditions enabling binding of the targets to recognition moieties; and
(ii) determining conductance in each assay set.

42. A method according to ~~any one of Claims 24 to 26~~ wherein the level of conductance between said at least two electrodes is a measure of the
15 concentration of the target in the sample.